Status of the Claims

1. (Previously Amended) A method for making a hypermutable, antibody-producing cell *in vitro*, comprising introducing into a cell that produces antibodies a polynucleotide comprising a dominant negative allele of a mismatch repair gene, wherein said dominant negative allele is a truncation mutant of a PMS2, wherein said antibody-producing cell becomes hypermutable.

2. (Original) The method of claim 1 wherein said polynucleotide is introduced by transfection of a suspension of cells *in vitro*.

3. (Canceled)

4. (Original) The method of claim 1 wherein said mismatch repair gene is human *PMS2*.

5-9. (Canceled)

10. (Previously Amended) The method of claim 1 wherein said allele comprises a truncation mutation at codon 134.

11. (Original) The method of claim 10 wherein said truncation mutation is a thymidine at nucleotide 424 of wild-type *PMS2*.

12-21. (Canceled)

22. (Previously Amended) The method of claim 1 wherein an immunoglobulin gene is co-introduced into said cell, whereby said cell produces said antibodies.

23. (Previously Amended) A homogeneous culture of isolated, hypermutable, mammalian cells wherein said cells produce antibodies and comprise a dominant negative allele of a mismatch repair gene, wherein said dominant negative allele encodes a truncation mutant of a PMS2 protein.

24. (Canceled)

25. (Previously Amended) The culture of isolated, hypermutable, mammalian cells of claim 23 wherein the mismatch repair gene is human *PMS2*.

26-28. (Canceled)

29. (Previously Amended) The culture of isolated, hypermutable, mammalian cells of claim 23 wherein the cells express a protein consisting of the first 133 amino acids of hPMS2.

30-72. (Canceled)

73. (Currently Amended) [[A]] <u>An isolated, hypermutable, antibody-producing</u> cell produced by the method of claim 1.

74. (Currently Amended) [[A]] <u>An isolated, hypermutable, antibody-producing</u> cell

produced by the method of claim 4.

75. (Previously added) The method of claim 1 further comprising the step restoring genetic stability of said hypermutable cell.

76. (Currently Amended) [[A]] An isolated, genetically stable, mutated antibody-producing cell produced by the method of claim 75, wherein said isolated, genetically stable, mutated antibody-producing cell produces an antibody having increased affinity for antigen relative to said antibody-producing cell prior to introduction of said dominant negative allele of said mismatch repair gene, wherein said dominant negative allele of said PMS2 mismatch repair gene of said polynucleotide is inactivated.

77. (Currently Amended) A homogeneous culture of the isolated, genetically stable, antibody-producing cells of claim 76.

78. (Previously added) The method of claim 22 further comprising the step restoring genetic stability of said hypermutable cell.

79. (Currently Amended) [[A]] An isolated, genetically stable, mutated antibody-producing cell produced by the method of claim 78, wherein said isolated, genetically stable, mutated antibody-producing cell produces an antibody having increased affinity for antigen relative to said antibody-producing cell prior to introduction of said dominant negative allele of said mismatch repair gene, wherein said dominant negative allele of said PMS2 mismatch repair gene of said polynucleotide is inactivated.

80. (Currently Amended) A homogeneous culture of the isolated, genetically stable, mutated antibody-producing cells of claim 79.

81. (New) An isolated, genetically stable, mutated antibody-producing cell produced by the method of claim 75, wherein said isolated, genetically stable, mutated antibody-producing cell produces an increased titer of antibody relative to said antibody-producing cell prior to introduction of said dominant negative allele of said mismatch repair gene, wherein said dominant negative allele of said PMS2 mismatch repair gene of said polynucleotide is inactivated.

82. (New) A homogeneous culture of the isolated, genetically stable, mutated antibody-producing cells of claim 81.

83. (New) An isolated, genetically stable, mutated antibody-producing cell produced by the method of claim 78, wherein said isolated, genetically stable, mutated antibody-producing cell produces an increased titer of antibody relative to said antibody-producing cell prior to introduction of said dominant negative allele of said mismatch repair gene, wherein said dominant negative allele of said PMS2 mismatch repair gene of said polynucleotide is inactivated.

84. (New) A homogeneous culture of the isolated, genetically stable, mutated antibody-producing cells of claim 83.